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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/057,467

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Garry P. Nolan

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04/11/2005

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EXAMINER

BRUSCA, JOHN S

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 04/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/057,467

Applicant(s)

NOLAN, GARRY P.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 8-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The rejection of claims 8-25 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement in the Office action mailed 15 November 2004 is withdrawn in view of the amendment to the claims filed 15 February 2005.

### *Claim Rejections - 35 USC § 103*

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 8-10, 12-19, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. in view of Rayner et al. in view of Gonda et al.

The claims are drawn to a method of screening for phenotypes in cells comprising a library of retroviral vectors comprising random sequences that express peptides comprising an amino-terminal glycine. In some embodiments the random sequences are sequenced after selection and isolation, the cells are mammalian cells, the library comprises up to  $10^9$  members, and the inserts are linked to a fusion partner. In some embodiments the phenotype is cell growth or cell death.

Kauffman et al. shows in the abstract and throughout the use of libraries of expression vectors encoding random polypeptides to screen for desired phenotypes. Kauffman et al. shows in column 1 that their method may be used to select for a wide range of properties conferred by the random peptide. Kauffman et al. shows in column 2, lines 13-16 that the expression vector can be viral and the host cell can be a eukaryotic cell. Kauffman shows in column 3, lines 45-56 that beta galactosidase fusion proteins linked to the random sequence have advantages in allowing for purification of the protein. Kauffman et al. shows in column 8, lines 20-22 that the library can have up to a billion members. Kauffman et al. shows in column 12-13 selection of phenotypic properties that affect the survival of the host cell, and selection of polypeptides that catalyze a desired reaction or regulate gene expression in vivo. Kauffman et al. does not show use of retroviral vectors, use of a glycine N-terminal to the randomized insert, use of mammalian host cells, or sequencing the selected inserts.

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Rayner et al. shows retroviral vector cDNA libraries in the abstract and throughout.

Rayner et al. shows on page 880 that retroviral vectors have advantages of efficiency and stable integration and expression, and allow for selection of phenotypes of infected cells. Rayner et al. show a cDNA library in their retroviral vector with  $1.5 \times 10^6$  members on page 882. Rayner et al. shows screening infected mammalian T cells for acquisition of the phenotype of granulocyte-macrophage colony-stimulating factor (GM-CSF) independence in table 2. The sequence of isolated cells with the desired phenotype was determined as shown on page 885, and resulted in confirmation that IL-3 or GM-CSF expressing retroviral library members were in the selected cells. Rayner et al. concludes on page 886 that their method has general utility for isolation of any cDNA for which a functional screen can be devised, including differentiation along pathways that are not normally shown by a particular cell type.

Gonda et al. shows in the abstract and throughout that the amino terminal amino acid of a polypeptide controls the stability of the polypeptide in mammalian reticulocytes. Gonda et al. shows that glycine is among the set of amino acids that confer the highest stability to polypeptides.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Kauffman et al. by use of mammalian cells and retroviral vectors because Rayner et al. shows that retroviral vectors are advantageous to screen libraries in mammalian cells because they are efficient and stably integrated. It would have been further obvious to sequence the selected clones to further characterize the insert because Rayner et al. shows use of sequencing to characterize selected inserts. It would have been further obvious to construct the libraries of random peptides to contain an amino-terminal glycine

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residue because Gonda et al shows that amino-terminal glycines confer stability to polypeptides in mammalian cells.

6. Claims 8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above, and further in view of Scott et al. (cited in the Information Disclosure Statement filed 09 May 2002).

The claims are drawn to a method of using of presentation structures in random peptide libraries.

Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above do not show a method of using presentation structures in random peptide libraries.

Scott et al. reviews random peptide libraries. Scott et al. shows the use of presentation structures to facilitate activity of the random peptide insert on page 40.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the vectors of Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above by use of a presentation structure because Scott et al. shows that presentation structures help enhance the activity of random peptide inserts.

7. Claim 8, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above, and further in view of Garcia-Bustos et al.

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The claims are drawn to a method of using a library comprising nuclear localization signal peptides fused to random peptides.

Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above does not show a method of using a library comprising nuclear localization signal peptides fused to random peptides.

Garcia-Bustos et al. reviews nuclear localization signals. Garcia-Bustos et al. shows on pages 84-85 that fusion of a nuclear localization signal to a protein directs the protein to localize to the cellular nucleus.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the proteins of Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above by addition of a nuclear localization signal so that activities of the proteins in cell nuclei could be assayed.

8. Claims 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above, and further in view of Abbas et al.

The claims are drawn to a method of using a library of random peptides to modulate cellular differentiation. In some embodiments the differentiation markers are characteristic of T-cells or B-cells.

Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above does not show alterations of differentiation markers that are characteristic of T cell or B cell activation.

Abbas et al. reviews T cell and B cell differentiation particularly on pages 236-239.

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It would have been obvious to a person of ordinary skill in the art at the time the invention was made to extend the screening of phenotypes of Kauffman et al. in view of Rayner et al. in view of Gonda et al. as applied to claims 8-10, 11-19, 21, and 22 above to determine states of differentiation of T cells and B cells because Abbas et al. shows that such differentiation is important in the function of the immune system, and such screening would allow researchers to gain further insights into the mechanisms of regulation of differentiation of T cells and B cells.

### ***Conclusion***

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is



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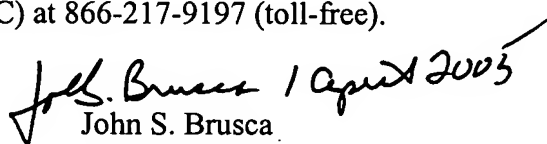
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For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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John S. Brusca  
Primary Examiner  
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